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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,855	02/27/2002	Evan C. Unger	UNGR-1632	8641
7590	10/20/2004		EXAMINER	
Woodcock Washburn LLP One Liberty Place - 46th Floor Philadelphia, PA 19103			SHARAREH, SHAHNAM J	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.	10/084,855	Applicant(s)	UNGER, EVAN C.
Examiner	Shahnam Sharareh	Art Unit	1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1)  Responsive to communication(s) filed on 08 July 2004.
- 2a)  This action is FINAL. 2b)  This action is non-final.
- 3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4)  Claim(s) 1,47,49-51 and 55 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5)  Claim(s) \_\_\_\_\_ is/are allowed.
- 6)  Claim(s) 1,47,49-51 and 55 is/are rejected.
- 7)  Claim(s) \_\_\_\_\_ is/are objected to.
- 8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9)  The specification is objected to by the Examiner.
- 10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a)  All
  - b)  Some \*
  - c)  None of:
    1.  Certified copies of the priority documents have been received.
    2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1)  Notice of References Cited (PTO-892)
- 2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3)  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/23/2004.
- 4)  Interview Summary (PTO-413) Paper No(s)/Mail Date. \_\_\_\_\_.
- 5)  Notice of Informal Patent Application (PTO-152)
- 6)  Other: \_\_\_\_\_.

### **DETAILED ACTION**

Amendment filed on July 08, 2004 is entered. Claims 1, 47-59 are pending. Any rejection that is not addressed in this Office Action is considered withdrawn in view of the amendment.

#### ***Election/Restrictions***

Applicant's election of the species in which the lipid is a combination of at least one phosphatidylcholine, at least one phosphatidylethanolamine, and at least one phosphatidic acid; the gas is perfluorocarbon gas and the oil is triacetin in Paper No. 10 is acknowledged. Claims 1, 47, 49-51, 55 read on the elected species. Accordingly, the claims are searched and examined at least to the extent that they read on the elected species until an allowable subject matter is found.

#### ***Double Patenting***

Claims 1, 47, 49-51, 55 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-102 of U.S. Patent No. 6,146,657 (US '657), claims 111-173 of U.S. Patent No. 6,139,819 (US '819), claim 95 of US Patent No. 6,071,494 (US '494), claims 57-122 of U.S. Patent 6,414,139 (US '139). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the patented claims are directed to compositions comprising gaseous liposomes, a bioactive agent, and a surfactant, wherein the gas is a perfluorocarbon.

Applicant arguments with respect to this rejection have been fully considered but are not persuasive. Applicant appears to be arguing that the instant compositions contain

oil that can further encapsulate the gas, and such feature would not have been obvious to one of ordinary skill in the art. see Arguments at pg 8, 1<sup>st</sup> para.

In response Examiner states that as explained in the previous Office Action, selecting an oil to improve the stability of a bioactive agent is well within the level of ordinary skill in the art and further is a function of the bioactive agent employed with the therapeutic system. Once the oil is selected to improve solubility of bioactive agents, it would function the same as instantly claimed, because the liposomes of the cited patents are prepared in the same manner as those instantly claimed. Applicant has not provided any evidence to the contrary. Therefore, the rejection is maintained.

***Claim Rejections - 35 USC § 102***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 47, 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Grinstaff et al US Patent 5,498,421 ("Grinstaff").

Applicant's arguments have been fully considered but are not persuasive. Applicant argues that Grinstaff cannot anticipate claims 1, 47, 51 because it does not explicitly or implicitly teach all elements of the claimed invention. see Arguments at pg. 8, 2<sup>nd</sup> para. Applicant further adds that the limitation of "said oil further encapsulates said gas or gaseous precursor," is not disclosed in Grinstaff. *Id.*

In response Examiner states that Applicant has not met the burden of proof to show that Grinstaff's composition does not meet all elements of the instant compositions. As the initial matter, Grinstaff discloses compositions comprising a

Art Unit: 1617

biologic agent, a polymeric shell encapsulating a perfluorocarbon gas and an oil. see Grinstaff at col 12, lines 10-40. Grinstaff clearly teaches the use of suitable oil to dissolve his bioactive agents (see col 25, lines 3-20). Grinstaff adds that his polymeric shell contain contains diagnostic agent, such as a gas, in a dispersing agent. see col 12, lines 34-45, col 54, lines 30-36. Grinstaff then claims that the dispersing agent can be a soybean oil, olive oil, etc... see col 55, lines 47-25. Grinstaff also states that when such dispersing agent is used, the oil is within the shell surrounding the diagnostic or biologic agent. see col 32, lines 11-35.

Second, the scope of the instant oils is directed to various possibilities as the oil including synthetic oils or fatty acids. see instant claim 51. Grinstaff clearly teaches the use of such synthetic oils encompassed by the instant claims. see col 25, lines 33-36; col 55, lines 55-61.

Additionally, Grinstaff prepares his microemulsion by vigorously mixing the components of his microemulsion together. see example 1. Such process step is viewed to be analogous to those employed in the instant application for formulating the instantly claimed targeted delivery system, because they both employ steps to vigorously mix the components of their mixtures. Therefore, the final product created by both methods must be the same as well.

Since the material used by Grinstaff is the same as those employed in the instant delivery system; in conjunction with the fact that Grinstaff's method of making is substantially the same as the instant methods, Examiner has taken the position that the shells of Grinstaff is the same as the instant targeted delivery systems of claims 1, 47,

51. Applicant has not provided any evidence or show such evidence on the record as to how the Grinstaff's shells that entrap gas and is dispersed in the oil, is functionally or structurally different from the claimed delivery systems. Accordingly, Applicant has not met the burden to overcome the rejection of record.

***Claim Rejections - 35 USC § 103***

Claims 1, 47, 49-51, 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klaveness US Patent 6,261,537 ("Klaveness").

The instant claims are directed to compositions comprising a therapeutic agent, a lipid microsphere encapsulating a gas and an oil. The scope of the instant oils is broad and directed to various possibilities as the oil including synthetic oils or fatty acids. see instant claim 51. Accordingly, any oil of prior art that falls within the scope of instant oil and is used in combination with a gas and a lipid microsphere, is viewed to encapsulate the gas.

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Klaveness teaches the use of microbubbles in combination with a therapeutic. see abstract, col 40-49. Klaveness discloses targeted compositions comprising phospholipid-stabilized gas microbubbles and a therapeutic agent. see abstract. Klaveness teaches the use of suitable phospholipids such as one phosphatidylcholine, phosphatidylethanolamine, and phosphatidic acids. see col 5, lines 10-35. Klaveness describes the use of perfluorocarbon gas. see col 4, lines 25-55; col 117, lines 1-30; col 118, lines 20-30. Klaveness teaches the use of any suitable lipids such as stearic acids, palmitic acids, or other suitable surfactants which fall within the scope of the instant oils.

see col 6, lines 14-30. Klaveness also teaches the use of triacetin. see col 59, line 25.

Klaveness fails to explicitly use triacetin in his compositions.

Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention to use any triacetin with the microbubbles of Klaveness, because as suggested by Klaveness, the ordinary skill in the art would have had a reasonable expectation of success in delivering such agent in combination with a stabilized lipid microsphere to a target of interest to improve clinical efficacy.

### ***Conclusion***

No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action, because it modifies the scope of the claim with respect to the components used and the manner they are combined. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
RUSSELL TRAVERS  
PRIMARY EXAMINER

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